In the Claims:

Please cancel claims 50-55 without prejudice.

Please amend claim 35 as follows:

35. **(Amended)** A method for identifying a compound that modulates an immune response, comprising

providing an indicator composition comprising a maf family protein and a target DNA to which said maf family protein binds, said indicator composition being an indicator cell or an acellular preparation;

contacting the indicator composition with each member of a library of test compounds;

selecting from the library of test compounds a compound of interest that modulates the activity of the maf family protein; and

determining the effect of the compound of interest on an immune response to thereby identify a compound that modulates an immune response.

REMARKS

Claims 35-55 were pending in the application. Claims 50-55 have been cancelled herein without prejudiced as being directed to a non-elected invention. Claim 35 has been amended to correct a grammatical error. Accordingly, following entry of the amendments presented herein, claims 35-49 will be pending. For the Examiner's convenience, a copy of the claims as they will be pending upon entry of the present amendment, is set forth herein as Appendix A.

Attached hereto is a marked-up version of the changes made to the claims by the current amendments. The attached page is captioned "Version With Markings to Show Changes Made".

No new matter has been added. The foregoing claim amendments and cancellations should in no way be construed as an acquiescence to any of the Examiner's rejections, and have been made solely to expedite the prosecution of the application.

Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Double Patenting

The Examiner has rejected claim 38 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 13 of U.S. Patent No. 5,958,671 (the '671 patent). Specifically the Examiner is of the opinion that "although the conflicting claims are not identical, they are not patentably distinct from each other . . .."

Applicants respectfully disagree. However, in the interest of expediting prosecution, Applicants submit herewith a Terminal Disclaimer over the '671 patent. Accordingly, Applicants respectfully request withdrawal of the double patenting rejection over the '671 patent.

Rejection of Claims 35-49 Under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 35-49 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner is of the opinion that

> The only maf family protein described in the specification or prior art to be associated with a cell involved in immune response is c-Maf. The instant specification describes c-Maf as being a positive regulator of IL-4 transcription in Th2 cells. There is no description of any maf family protein being involved in expression of any other cytokine genes from any cell type.

The Examiner concludes that "[g]iven the lack of description from the specification for immune response assays, the lack of an adequate description of what constitutes a "maf family" protein, and the lack of description of any maf family polypeptide in the specification or prior art which is involved in any clear way with an immune response, except for c-Maf and IL-4 expression, one of skill in the art would not be able to envision

a representative number of the methods of the claimed invention. Therefore, one of skill in the art would reasonably conclude that applicants were not in possession of the claimed invention."

Applicants respectfully traverse this rejection. Applicants submit that there is sufficient written description in Applicants' specification to inform a skilled artisan that Applicants were in possession of the claimed invention at the time the application was filed, as required by 35 U.S.C. §112, first paragraph (see M.P.E.P. 2163.02). Contrary to the Examiner's assertion, Applicants describe, in detail, the genus of maf proteins encompassed by the pending claims. For example, at least on page 7, line 32 to page 8, line 22, Applicants specifically describe that:

> The maf family of proteins is a sub-family of AP-1/CREB/ATF proteins. . . . V-*maf* encodes a 42 kd basic region/leucine zipper (b-zip) protein with homology to the *c-fos* and *c-jun* oncogenes. Its cellular homologue, the *c-maf* proto-oncogene has only two structural changes in the coding region from v-maf (Kataoka, K. *et al.* (1993) *J. Virol.* 67:2133-2141). The maf family includes *c-maf, mafB*, a human retina-specific gene *Nrl* (Swaroop, A. *et al.* (1992) *Proc. Natl. Acad. Sci. USA* 89:266-270), *mafK, mafF, mafG* and *p18.* The latter four, *mafK, mafF, mafG* and *p18,* each encode proteins that lack the amino terminal two thirds of c-Maf that contains the transactivating domain (Fujiwara, K.T. *et al.* (1993) *Oncogene* 8:2371-2380; Igarashi, K. *et al.* (1995) *J. Biol. Chem.* 270:7615-7624; Andrews, N.C. *et al.* (1993) *Proc. Natl. Acad. Sci. USA* 90:11488-11492; Kataoka, K. *et al.* (1995) *Mol. Cell. Biol.* 15:2180-2190) and are referred to herein as "small" mafs. C-maf and maf family members form homodimers and heterodimers with each other and with Fos and Jun, consistent with the known ability of the AP-1 proteins to pair with each other (Kerppola, T.K. and Curran, T. (1994) *Oncogene* 9:675-684; Kataoka, K. *et al.* (1994) *Mol. Cell. Biol.* 14:700-712). The DNA target sequence to which c-Maf homodimers bind, termed the c-Maf response element (MARE), is a 13 or 14 bp element which contains a core TRE (T-MARE) or CRE (C-MARE) palindrome respectively. Prior to the present invention, little was known about the function of maf family members, although c-Maf has been shown to stimulate transcription from the Purkinje neuron-specific promoter L7 (Kurscher, C. and Morgan, J.I. (1994) *Mol. Cell. Biol.* 15:246-254) and Nrl has been shown to drive expression of the QR1 retina-specific gene (Swaroop, A. *et al.* (1992) *Proc. Natl. Acad. Sci. USA* 89:266-270). The small mafs have been shown to function as repressors of α and β-globin transcription when bound as homodimers but are essential as heterodimeric partners with the erythroid-specific factor p45NF-E2 to activate globin gene transcription (Kataoka, K. *et al.* (1995) *Mol. Cell. Biol.* 15:2180-2190; Igarashi, K. *et al.* (1994) *Nature* 367:568-

572). MafK overexpression has been shown to induce erythroleukemia cell differentiation (Igarashi, K. *et al.* (1995) *Proc. Natl. Acad. Sci. USA* 92:7445-7449).

Thus, Applicants describe the representative members of the genus of maf proteins in terms of both structural and functional features which are common to a substantial portion of the genus, thus evidencing that Applicants were in possession of the invention as required by 35 U.S.C. § 112, first paragraph.

The Examiner further states that the prior art does not describe the maf protein family's involvement in the immune response. Applicants point to page 8, lines 22-24, wherein Applicants explicitly state that "prior to the present invention, there have been no reports implicating *c-maf* or maf family members in the regulation of genes expressed in lymphoid cells or in cytokine gene expression in any tissue." Accordingly, it follows that the prior art does not disclose the relationship between the maf family of proteins and modulation of the immune response.

Furthermore, contrary to the Examiner's assertion, Applicants' disclosure does provide a description of immune response assays encompassed by the pending claims. Applicants direct the Examiner's attention to pages 36-40 wherein Applicants describe various screening assays which can be used to identifying a compound that modulates an immune response. For example, Applicants teach a two-hybrid assay system and a single-hybrid assay system to identify modulators of the immune response. Applicants also specifically describe the recombinant expression vectors, the reporter genes and the cell types that can be used in the screening assays encompassed by the pending claims. (See page 36-37). Additionally, the skilled artisan could have determined the effect of a compound of interest on an immune response using conventional techniques. Such conventional techniques are described, in detail, in, for example, Sambrook, J. *et al.*. (1989) *Molecular Cloning: A Laboratory Manual-2nd.* Cold Spring Harbor Laboratory Press, Cold Spring Harbor New York, USA (incorporated by reference on page 35, lines 15-16).

Accordingly, Applicants respectfully conclude that the specification describes several exemplary species of the claimed genus of maf proteins, and also describes several exemplary assays to screen for modulation of the immune response, evidencing

that Applicants were in possession of the claimed invention at the time of filing as required by 35 U.S.C. § 112, first paragraph. The Regents of the University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 35-49 under 35 U.S.C. § 112, first paragraph.

If the Examiner insists on maintaining this rejection, the Examiner is respectfully requested to present evidence or reasons why persons skilled in the art would not recognize in Applicants' disclosure a description of the invention as defined by the pending claims.

Rejection of Claims 35-49 Under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 35-49 under 35 U.S.C. §112, first paragraph, because "the specification, while being enabling for embodiments wherein the immune response monitored is the immune response assayed is the effect of the test compound on expression of a an interleukin-4 gene and wherein the maf family protein is c-Maf, does not reasonably provide enablement for practicing the claimed invention with any other immune response and with any other maf family proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims."

Applicants respectfully traverse the foregoing rejection on the grounds that the claimed invention is fully enabled by the disclosure in Applicant's specification. As set forth above, Applicants' disclosure does provide a description of immune response assays encompassed by the pending claims. Applicants direct the Examiner's attention to pages 36-40 wherein Applicants describe various screening assays which can be used to identifying a compound that modulates an immune response. For example, Applicants teach a two-hybrid assay system and a single-hybrid assay system to identify modulators of the immune response. Applicants also specifically describe the recombinant expression vectors, the reporter genes and the cell types that can be used in the screening assays encompassed by the pending claims. (See page 36-37). Additionally, Applicants submit that the step the Examiner specifically rejects as not enabled, *i.e.*, the step of determining the effect of the compound of interest on an immune response to thereby

identify a compound that modulates a immune response, was routine to one of ordinary skill in the art at the time of the present invention and would not require undue experimentation. For example, the skilled artisan could have determined the effect of a compound of interest on an immune response using conventional techniques. Such conventional techniques are described, in detail, in, for example, Sambrook, J. *et al.*. (1989) *Molecular Cloning: A Laboratory Manual-2nd.* Cold Spring Harbor Laboratory Press, Cold Spring Harbor New York, USA (incorporated by reference on page 35, lines 15-16).

Applicants submit that the Examiner's position, in effect, imposes an additional requirement, one not contained in 35 U.S.C. §112, of a working example or examples to enable the breadth of the claims. Applicants assert that a working example is not required to enable the breadth of the pending claims and that "there is no magical relation between the number of representative examples and the breadth of the claims". In re Borkowski and VanVenroy, 164 U.S.P.Q. 642, 646 (C.C.P.A. 1970). In fact, § 112 only requires that the "specification contain a written description of the invention, and the manner and process of making and using it".

The key question then, is whether it would require undue experimentation to conduct Applicants' methods as broadly claimed. As the Examiner is aware, enablement is not precluded by the necessity for some experimentation, and a considerable amount of experimentation is permitted. See In re Wands, 8 U.S.P.Q. 2d 1400, 1404 (Fed. Cir. 1988). Accordingly, it is Applicants' position that based on the teachings of the specification and the knowledge in the art, the ordinarily skilled artisan would be able to make and use the claimed methods without undue experimentation. Applicants therefore request reconsideration and withdrawal of the rejections of claims 35-49 under 35 U.S.C. § 112, first paragraph.

Rejection of Claims 35-49 Under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 35-49 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner rejects claim

35 as being grammatically incorrect and rejects claims 35, 37-39 and 41-49 as indefinite for the recitation of "maf family proteins".

Applicants have amended claim 35 to read "said maf family protein binds" thereby obviating the rejection of this claim as being grammatically incorrect.

With respect to the rejection of claims 35, 37-39 as being indefinite for the recitation of "maf family proteins", Applicants respectfully traverse. To satisfy the standard of definiteness under 35 U.S.C. § 112, second paragraph, the Applicants must merely "convey with reasonable clarity to those skilled in the art, as of the filing date sought, he or she was in possession of the invention." (MPEP § 2163.02) As set forth above in detail, Applicants specification, at pages 7-8, clearly define maf family proteins. Furthermore, Example 2, at page 41 of the instant specification, exemplifies isolation of a representative member of the maf family of proteins, *i.e.*, c-maf. Applicants submit Applicants disclosure renders the description of the maf family proteins sufficiently definite.

Accordingly, Applicants request reconsideration and withdrawal of the rejection of claims 35-49 under 35 U.S.C. § 112, second paragraph.

CONCLUSION

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,

LAHIVE & COCKFIELD, LLP

By _____
Cynthia L. Kanik, Ph.D.
Attorney for Applicants
Reg. No. 37,320

LAHIVE & COCKFIELD, LLP
28 State Street
Boston, MA 02109
Tel. (617) 227-7400

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 35 was amended as follows:

35. A method for identifying a compound that modulates an immune response, comprising

providing an indicator composition comprising a maf family protein and a target DNA to which said maf family protein ~~bind~~ binds, said indicator composition being an indicator cell or an acellular preparation;

contacting the indicator composition with each member of a library of test compounds;

selecting from the library of test compounds a compound of interest that modulates the activity of the maf family protein; and

determining the effect of the compound of interest on an immune response to thereby identify a compound that modulates an immune response.

APPENDIX A

35. A method for identifying a compound that modulates an immune response, comprising

providing an indicator composition comprising a maf family protein and a target DNA to which said maf family protein ~~bind~~ binds, said indicator composition being an indicator cell or an acellular preparation;

contacting the indicator composition with each member of a library of test compounds;

selecting from the library of test compounds a compound of interest that modulates the activity of the maf family protein; and

determining the effect of the compound of interest on an immune response to thereby identify a compound that modulates an immune response.

36. The method of claim 35, wherein the maf family protein is c-Maf.

37. The method of claim 35, wherein the effect of the compound of interest on an immune response is determined by determining the effect of the compound on expression of a Th2-associated cytokine gene.

38. The method of claim 37, wherein the Th2-associated cytokine gene is an interleukin-4 gene.

39 The method of claim 35, wherein the effect of the compound of interest on an immune response is determined by determining the effect of the compound on development of T helper type 1 (Th1) or T helper type 2 (Th2) cells.

40. The method of claim 35, wherein the maf family protein is selected from the group consisting of v-maf, mafB, Nrl, mafK, mafF, mafG and p18.

41. The method of claim 35, wherein the target DNA comprises a regulatory sequence of a Th2-associated cytokine gene.

42. The method of claim 41, wherein the Th2-associated cytokine gene is an interleukin-4 gene.

43. The method of claim 35, wherein the indicator composition is an indicator cell.

44. The method of claim 43, wherein the indicator cell is a lymphoid cell.

45. The method of claim 44, wherein the lymphoid cell is a Th2 cell.

46. The method of claim 44, wherein the lymphoid cell is a Th1 cell.

47. The method of claim 44, wherein the lymphoid cell is a B cell.

48. The method of claim 43, wherein the indicator cell is a non-lymphoid mammalian cell.

49. The method of claim 43, wherein the indicator cell is a yeast cell.